84-2 - Salmonella Mutagenicity Test

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DATA EVALUATION REPORT

Study Type: Gene Mutation in Bacteria

TOX. CHEM. No.: 298C

Accession No.: 7E3489

MRID No.:

Test Material: CGA 154281 (FL 860318)

Study Number(s): 86076 (MIN 862200)

Sponsor: CIBA-GEIGY Corp.

Test Facility: Division of Toxicology/Pathology, CIBA-GEIGY Corp.

Title of Report: Salmonella/Mammalian-Microsome Mutagenicity Assay

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Report Issued: October 17, 1986

Conclusions:

CGA 154281 Technical is mutagenic in Ames assay at the concentration of 1000 ug/plate in the presence and absence of metabolic activation.

Concentrations tested: 5, 10, 50, 250, and 1000 ug/plate.

Classification of Data: Acceptable

PC 91509

Title of Report: Salmonella/Mammalian-Microsome Mutagenicity Test with CGA 154261 Technical

Procedure:

Five histidine-requiring strains of Salmonella typhimurium (TA98, TA100, TA1535, TA1537, and TA1538) were used in this study.

The mutagenicity of CGA 154281 Technical dissolved in DMSO at predetermined concentrations (i.e., 5, 10, 50, 250, and 1000 ug/plate) was evaluated by the Ames Salmonella/Mammalian-Microsome Mutagenicity Test (Mutation Res. 31, 347-364, 1975) in the presence and absence of exogenous metabolic activation (S-9 mix). The commercial S-9 liver microsomal fraction prepared from Aroclor 1254-induced rats was obtained from Bionetics, Charleston, South Carolina and used in this study. Mutations were quantified on triplicate plates for each strain by counting His^+ revertant colonies after 48 hours of incubation at 37 C. on a histidine-deficient agar. If the compound is mutagenic, it would demonstrate at least 2-fold increase over the control value and also exhibited a dose-related increase in the number of histidine-independent colonies. Positive controls and solvent control were run concurrently with the test compound in this study.

Results:

Mean Number of His^+ Revertant Colonies Per Plate

Treatment	Conc. Per Plate	TA98		TA100		TA1535		TA1537		TA1538	
		-S9	+S9	-S9	+S9	-S9	+S9	-S9	+S9	-S9	+S9
DMSO		23	29	95	96	15	15	7	9	13	18
CGA 154281	5 ug	24	32	94	94	15	12	8	7	14	20
	10 "	23	29	98	100	15	11	8	8	11	16
	50 "	26	29	100	100	12	11	8	8	14	20
	250 "	35	36	98	104	10	17	12	13	23	29
	1000 "	77*	101*	106	113	10	13	19*	28*	87*	120*
Positive Controls:											
DNMC	2 ug	706*	-	-	-	-	-	-	-	42*	-
NaN_3	3 "	-	-	733*	-	-	-	-	-	-	-
	0.3 "	-	-	-	-	192*	-	-	-	-	-
9-NH_2-Acridine	40 "	-	-	-	-	-	-	113*	-	-	-
BP	3 "	-	338*	-	737*	-	-	-	-	-	141*
B-NPLM	10 "	-	-	-	-	-	376*	-	-	-	-
3-CH_3-Cholanthrene	10 "	-	-	-	-	-	-	-	37*	-	-

* Significantly different from the solvent control: greater than 2-fold increase over the solvent control; DNMC = Daunomycin; BP = Benzo(a)-pyrene; B-NPLM = B-Naphthylamine.

Findings:

1. Based on the results obtained from the preliminary toxicity test, the concentration greater than 1000 ug/plate exhibited toxic and inhibitory properties to tester strain TA100. Therefore, the concentration of 1000 ug/plate was selected as the highest dose for this study.

2. The spontaneous revertant colonies for each of these five strains of Salmonella typhimurium (TA98, TA100, TA1535, TA1537, and TA1538) were found within the normal range of His- revertant colonies recommended by the Ames test (1975).

3. The strain specific control compounds (Daunomycin, NaN_3 and 9-Aminoacridine) and the positive control compounds to ensure the efficacy of the activation (Benzo-(a)-pyrene, B-naphthylamine, and 3-CH_3-Cholanthrene) in this study have given the positive responses as expected.

4. Significant increase in the number of revertant colonies was observed at the highest concentration (1000 ug/plate) in three tester strains (TA98, TA1537, and TA1538) both in the presence and absence of metabolic activation. These increases also exhibited a dose-response relationship.

Evaluation:

Under the test conditions reported, the test compound, CGA 154281 Technical is mutagenic in the Ames Salmonella/Mammalian-Microsome Mutagenicity test at the concentration of 1000 ug/plate. However, a minor deficiency with respect to the density of grown cultures (i.e., 1-2 x 10^9 cells per ml) in reporting of this study was noted. This study is considered acceptable.